

8) (Amended) The compound of claim 7 wherein the compound is amphipathic.

12) (Amended) A process for forming a compound having a labile disulfide bond for use with an organism, comprising:

- a) forming the compound having a disulfide bond consisting of (i) a disulfide bond that is cleaved more rapidly than oxidized glutathione, and (ii) a disulfide bond constructed from thiols in which one of the constituent thiols has a lower pKa than glutathione, and (iii) a disulfide bond that is activated by intramolecular attack from a free thiol thereby forming two molecules derived from the compound;
- b) inserting the compound into the organism.

18) (Amended) The process of claim 12 wherein the compound is bifunctional.

### **REMARKS**

#### **Rejection of claims under 35 U.S.C. 112:**

Claims 7-14 and 18 have been rejected under §112, second paragraph. The claims have been amended to obviate the rejection.

Claims 7 and 12 have been amended to recite, “thereby forming two molecules derived from the compound.” The Office Action states that claim 7 is unclear to which two molecules the claim is directed. Applicants’ process involves a compound that is formed by attaching two separate molecules by a disulfide bond. When the disulfide bond is cleaved, the two molecules are released from each other. Applicants have amended claims 7 and 12 to clarify that the two molecules were part of the compound before separation.

The Action states that claim 8 is indefinite. Claim 8 has been amended to clarify the term compound as suggested.

Claim 18 has been amended to remove the term “molecule” since there is no antecedent basis as appropriately pointed out on page 3 of the Action.

Claims 7-14 and 18 have been rejected under §112, first paragraph. Applicants respectfully disagree.

On page 3 of the Action, last paragraph, it is suggested that new matter has been added in the form of the terminology “two molecules.” On page 4 the Action states that the terminology “a chemical bond between atoms is broken” may preclude the formation of two molecules instead of form 2 molecules as claimed. The Action further contends that there is no evidence that Applicants contemplated limiting the claims to the formation of two molecules.

Applicants point out that the specification on page 1, lines 19-23, states that the reversibility of a disulfide bond creates a transient attachment of two molecules. The words reversible and transient used in the specification clearly show the intent to cleave the disulfide bond thereby forming two molecules. On page 19, lines 5-10, under the heading Disulfide Bond Containing Bifunctional molecules, the specification discusses the reversibility of disulfide bond formation making them useful tools for transient attachment of two molecules. Again, transient is used to mean reversible. Therefore, if two molecules are transiently attached to form a compound, the attachment may be reversed to again form two molecules, as stated in the claims.

Applicants believe that the rejection is obviated based upon the clear intent shown in the specification to form two molecules from the compound.

Rejection of claims under 35 U.S.C. 102:

Claims 7-14 and 18 have been rejected under §102(b) as being anticipated by Wagner *et al.* Applicants respectfully disagree, however, they have amended the claims to make their process more clearly stated.

The Wagner *et al.* reference teaches a complex consisting of transferrin, which has disulfide bonds. However, unlike Applicants' labile disulfide, transferrin is N-acylated, is similar in structure to glutathione and has a similar pKa. Acylated nitrogen, found in glutathione and transferrin, is less electron withdrawing than Applicants' nitrogen, which results in Applicants' lower pKa. Therefore, transferrin is reduced at the same rate as glutathione and not considered labile (not reduced 3-15 times faster than oxidized glutathione) according to Applicants' definition. Similarly, a thiol of transferrin has a pKa like that of glutathione, which is 0.6 greater than the thiols formed by Applicants' process. Applicants have submitted a §132 Declaration with this Amendment and Response citing the pKa of N-acylated compounds and their similarity to the pKa of glutathione from the "Handbook of Biochemistry and Molecular Biology" a recognized authority.

Applicants have amended independent claims 7 and 12 to remove the Markush grouping. The claims now recite 3 steps that are required to describe the labile disulfide bond.

The rejection based upon Wagner *et al.* is believed to be overcome.

The reference to Stassen *et al.* is also believed to be overcome by the arguments presented above as well as by the amendment to remove the Markush grouping.

Applicants believe that claims 7-14 and 18 should be allowable over the cited prior art.

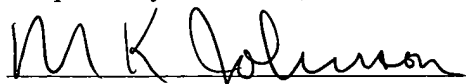
Rejection of claims under 35 U.S.C. 103:

Claims 7-14 and 18 have been rejected under §103(a) as being obvious when considering Wagner *et al.* and Lodish *et al.*

Arguments have been presented in response to the prior §102 rejection, which are also believed to obviate the §103 rejection.

The Examiner's objections and rejections are believed to be overcome by the amendments and response to the Office Action. In view of Applicants' amendments and discussion, it is submitted that independent claims 7 and 12 are allowable and therefore dependent claims 8-11 and 13, 14 and 18, which depend either directly or indirectly from the independent claims, should be allowable as well. Applicants respectfully request an early notice to such effect.

Respectfully submitted,



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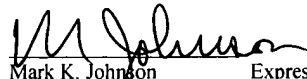
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